

Chemical shift in nuclear magnetic resonance phenomenon applied to study the kinetics of the hydrolysis of acetic anhydride

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With 4 figures in the text

Introduction

Physical methods such as conductivity measurements, polarography, spectrophotometry, dilatometry etc. have often been utilized for the study of kinetics of many chemical reactions. In such measurements variations are observed in some physical property of the system which changes as the chemical reaction proceeds. The recent developments in the nuclear magnetic resonance (n.m.r.) method and of microwave spectroscopy with its varied applications to several problems of physico-chemical interest suggest some possibilities of a new procedure to study the kinetics of chemical reactions. A necessary condition is that during the course of the reaction one of the reactants or products offers a characteristic parameter the changes of which are amenable to studies by n.m.r. or microwave spectroscopy. Already in the field of microwave absorption some chemical reactions in the gas phase at high temperatures [1] have been studied, e.g. the ionisation of the alkaline earth metals. The technique used was to measure the absorption of microwaves by free electrons from which, by use of Saha's thermal ionisation equation [2], the concentration of the free electrons was calculated.

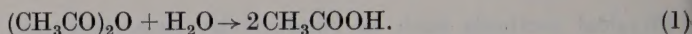
The possibilities of the application of nuclear magnetic resonance to study physico-chemical problems related to chemical reactions and equilibria were envisaged in the work of Arnold, Dharmatti and Packard [3] when they reported their successful work on the chemical effect on nuclear induction signals, resolving proton resonance lines in ethyl alcohol arising from different diamagnetic shielding of protons residing in different chemical environments.

The work of Hickmott and Selwood [4] applying the nuclear induction method to follow the kinetics of the reduction of trivalent europium by zinc in aqueous hydrochloric acid solution, was not concerned with the change of any parameter arising from what is called the "chemical shift" as embodied in the work of Arnold, Dharmatti and Packard just mentioned. Hickmott and Selwood observed the changes in the relaxation time (T_1) of protons (their experiment being done in aqueous solution) during the reduction by taking advantage of the difference in the effects of Eu^{3+} and Eu^{2+} on the thermal relaxation process. The effective magnetic moment, μ_{ion} of Eu^{2+} is 15 times greater than that of Eu^{3+} . Since T_1 is inversely proportional

to μ_{ion}^2 and to the ionic concentration, the relaxation effect may be considered solely due to Eu^{2+} . Thus $1/T_1$ gives an estimate of the concentration of Eu^{2+} . By measuring $1/T_1$ with time the kinetics of the reduction of trivalent europium was followed.

Another attempt in the application of the n.m.r. method to study the kinetics of an electron exchange reaction has been reported quite recently by Bruce, Norberg and Wiessman [5]. They have examined the reaction between tetramethyl *p*-phenylenediamine (TMPD) and Wurster's Blue (WB), the product derived from TMPD by one electron oxidation. They have studied the reaction by observing the "line-broadening" of the two chemically shifted proton resonance lines from ring protons and methyl protons of TMPD. Their experiment, however, was not concerned with any changes in the chemical shift during the reaction.

In our experiment to be described here we were interested to follow the chemical reaction by changes in chemical shift, in which a proton resonance line gradually "shifts" as the reaction proceeds. As no other work in this direction has yet been reported, we thought it worth while to compare the experimental findings on the reaction rate from nuclear magnetic resonance with an actual chemical experiment performed under the same conditions of temperature and concentrations of the reactants. The chemical reaction studied by us is the hydrolysis of acetic anhydride



This reaction, as many other organic reactions, is rather slow and it is therefore expected that some characteristics of the chemical shift of nuclear magnetic resonance lines arising from protons in different chemical groups should change as the reaction proceeds. Therefore the reaction may be amenable to be followed by the high resolution n.m.r.

The chemical shift in acetic acid has previously been studied by us from the point of view of dimerisation and hydrogen bonding [6]. The work of Cartwright and Monk [7] on the molecular association of some carboxylic acids in aqueous solutions from conductivity measurements and the recent work of Mackenzie and Winter [8], on the kinetics of chemical reactions in the solvo-system of acetic acid-acetic anhydride, may be mentioned here as in both works the question of dimerisation of acetic acid is advocated. Moreover the formation of a molecular complex between acetic acid and water seems to be well established from Raman spectroscopical and other work [9]. This complex formation and the dimerisation of acetic acid may well suggest that inferences drawn in regard to the hydrolysis of acetic anhydride based on eq. (1) may reflect an oversimplified picture of the reaction. However, in the presence of a solvent like water a preponderance of single molecules exists and thus the chemical reaction as stated in eq. (1) representing the formation of 2 moles of single molecules of acetic acid may be valid for the major part of the reaction until near its completion, where the concentration of acetic acid is high, the effect of dimerisation should arise. In the analysis of the experimental data and in the calculation of theoretical rate curves, however, we should consider the system as represented in eq. (1) without taking into account the formation and existence of molecular complexes.

The n.m.r. experiment and observations

The Purcell technique of nuclear magnetic resonance absorption was used to observe the chemically shifted proton resonance signals in the system of acetic

anhydride, water and acetic acid. The experimental method has been described in an earlier communication [10].

The magnetic field at which the experiment was performed was approximately 4930 gauss corresponding to the proton resonance frequency of 21 Mc/s. The absorption mode of the signals was observed as depicted in Fig. 1. The experiment was done at a room temperature which was kept constant at 27°C. The sample volume was about 0.02 cc. The liquid sample was contained in a small cylindrical glass tube of 2.4 mm inside diameter. Equimolar quantities of pure acetic anhydride and water were mixed in a small bottle and shaken for a few minutes. Immediately after the acetic anhydride and water were mixed two phases of the liquid system were obtained but after a few minutes' shaking a homogeneous solution was formed. A small quantity of the liquid was quickly passed through a capillary tube into the n.m.r. sample tube. The experimental observation of the nuclear magnetic resonance signal was made as quickly as possible. Thus the time this liquid system takes to form one homogeneous phase and the time to put the liquid in the n.m.r. probe ready for experiment imposes a time limit on recording the signals until after the lapse of a certain time after the reaction has started. Information about the position of the signals, or more precisely, the chemical shift of interest at $t = 0$, can be obtained by extrapolation of data for subsequent times.

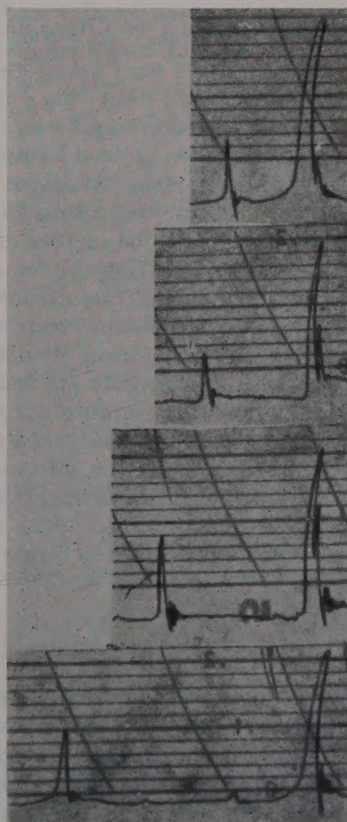


Fig. 1. Picture illustrating chemically shifted proton signals from the reacting system where the left-hand peak due to protons of water and the COOH group gradually recedes from the CH_3 proton peak, which appears on the right. The values of the externally applied magnetic field increase from the left to the right in the diagram.

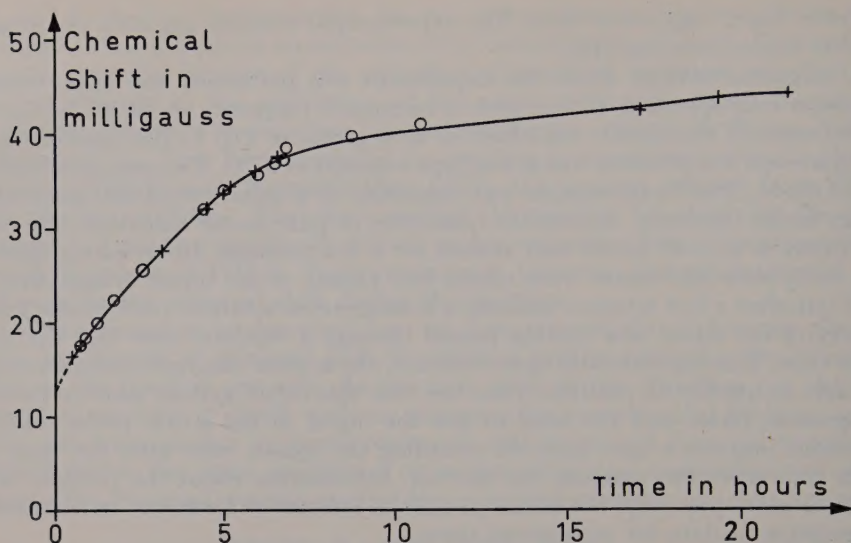


Fig. 2. Curve representing the chemical shift of the common peak due to protons of water and COOH group from that of CH_3 group of acetic acid and acetic anhydride plotted against time. o and + indicate readings from different runs.

The illustrative proton signals as the reaction proceeds are shown in Fig. 1, where signal amplitudes are plotted against externally applied magnetic field which increases from left to right. At lower values of the externally applied magnetic field the common peak due to protons from water and carboxyl groups occurs, since these protons are assumed to be rapidly exchanging (disregarding now molecular complex formation) and hence giving rise to an average diamagnetic shielding. The other peak on the right hand side of the picture which occurs at higher values of the externally applied magnetic field is due to protons of the methyl groups of acetic anhydride and acetic acid. The position of this peak, characteristic of the methyl group, does not change in the externally applied magnetic field plot during the experiment. As the reaction proceeds forming more acetic acid, the common peak progressively shifts towards the characteristic position for COOH group protons in pure acetic acid. This shift gives us the information of the quantity of acetic acid and water present at any time. Experimentally, the chemical shift between the CH_3 proton peak and the common proton peak due to water and COOH group of acetic acid is observed. This is presented in Table 1 and graphically in Fig. 2.

Analysis of the n.m.r. data

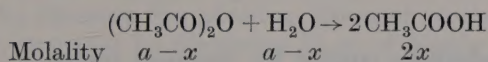
The procedure used to determine the mole fraction of acetic acid at any time from the chemical shift curve is as follows: The curve in Fig. 2 showing the chemical shift of the common peak (due to protons of water and of COOH group of acetic acid) from the CH_3 proton peak is extrapolated to the time $t = 0$, giving the position of the proton peak from water relative to that of the methyl peak. Hence for subse-

Table 1.

Time in minutes	Chemical shift in milligauss between CH ₃ peak and the common peak shifting with time (± 0.2 milligauss)	Time in minutes	Chemical shift in milligauss between CH ₃ peak and the common peak shifting with time (± 0.2 milligauss)
30	16.4	356	36.0
45	17.6	360	35.6
55	18.4	390	36.8
75	20.0	405	37.2
105	22.4	416	37.6
157	25.6	470	38.4
190	27.6	525	39.6
265	32.0	645	40.8
270	32.0	1 026	42.0
300	33.6	1 160	43.2
312	34.4	1 280	43.6

quent times the chemical shift of the common peak from the proton peak due to pure water can be determined. Now from Gutowsky and Saika's theory of chemical shift of aqueous electrolytes [11], the ratio of the chemical shift of the common peak at time t , from the peak at time $t=0$, to the chemical shift of the COOH peak in pure acetic acid from the peak at time $t=0$ is equal to the fraction of protons in COOH group in acetic acid at time t which are exchangeable between acetic acid and water. In a water molecule the number of exchangeable protons is two and in acetic acid it is one and if the molality of acetic acid is $2x$ and that of water $a-x$, the fraction of exchangeable protons in acetic acid is $2x/[2x+2(a-x)] = x/a$. (At $t=0$, when the reaction has not yet started and no acetic acid has formed, this ratio is zero and for time say $t=\infty$, when the reaction is complete, the ratio is one. The ratio x/a can therefore be determined from chemical shift data and since x/a is also the mole fraction of acetic acid at any time, as stated below, this quantity also is known. The mole fractions of acetic acid thus calculated are plotted against time in Fig. 3 and Fig. 4 and compared with the theoretical curves for first and second order reactions with different assumed values of the reaction rate constants k_I and k_{II} .

If we start with a moles of acetic anhydride and a moles of water per 1000 g of the solution and if we suppose that at time t , x moles of acetic anhydride and x moles of water have reacted, then $2x$ moles of acetic acid will be formed according to the equation



The mole fraction of acetic acid at time t is therefore x/a and that of water is $(a-x)/2a$.

For a first order reaction we have the relation

$$\ln \frac{a}{a-x} = k_I t \quad (2)$$

and for a second order reaction

$$\frac{x}{a(a-x)} = k_{II} t. \quad (3)$$

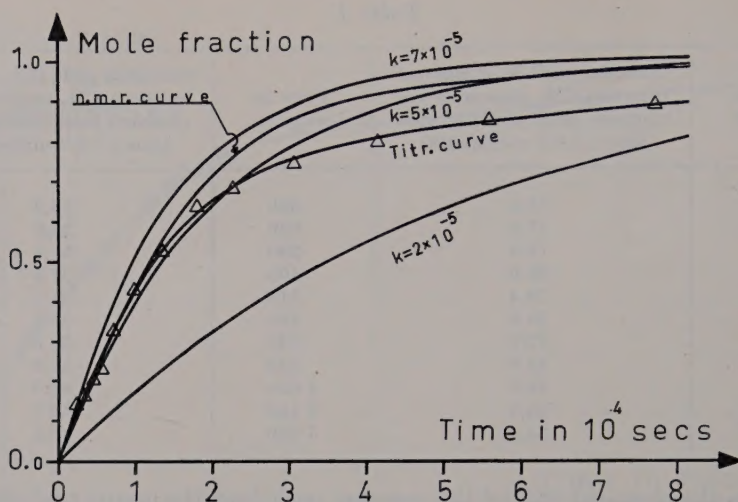


Fig. 3. Curves representing mole fraction of acetic acid present in the reacting system at any time as calculated from chemical shift data from the n.m.r. experiment and from the chemical experiment, compared with theoretical curves for a first order reaction with different assumed values of k_I . Δ indicates readings from chemical experiment.

As we know the initial concentration a we can determine the values of x at any time from eqs. (2) and (3) for the first and second order reactions with different assumed values of k_I and k_{II} . Since x is determined we can calculate the mole fraction of acetic acid, x/a , at any time for different values of k for first and second order reactions and thus the theoretical values can be obtained.

It appears that the n.m.r. curve is seen to be in better agreement with a first order than with a second order reaction curve. From the n.m.r. curve the value of the specific reaction rate k appears to be approximately $6 \times 10^{-5} \text{ sec}^{-1}$. A Powell plot [12] of relative concentration $[(a-x)/a]$ against the dimensionless time parameter $(ka^{n-1}t)$ also shows that the n.m.r. curve has the form which is in agreement with the form of a first order reaction curve. The chemical experiment curve, however, agrees with the form of a second order reaction, as will be discussed and presented below.

The hydrolysis studied by chemical methods

Extensive work has been done by several investigators (see references mentioned in the work of Gold [13]) to study the hydrolysis of acetic anhydride. In most cases chemical analysis has been used to determine the amount of acetic anhydride left unreacted in the solution after certain times. The rate constants have then been calculated in an analogous manner to the one described above.

Most of the earlier investigations were carried out in dilute aqueous solutions in which a pseudo-monomolecular reaction can be expected since the concentration of water remained constant. This first order reaction has been studied extensively to determine the effects of catalysis of different ions on the reaction rate.

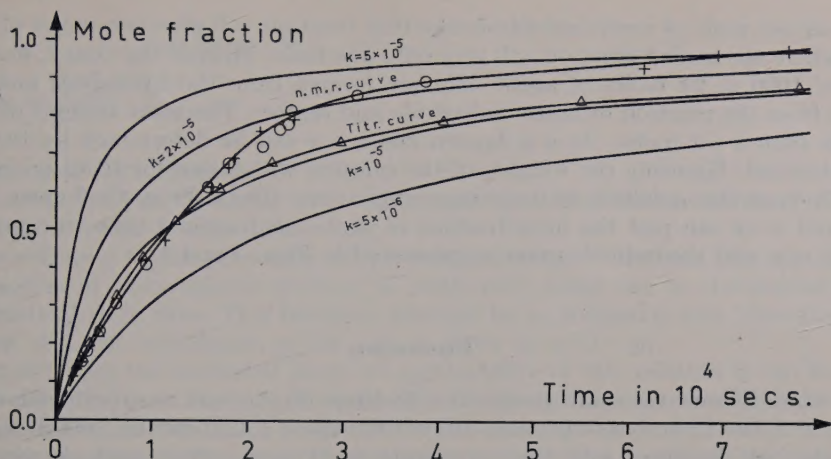


Fig. 4. Curves representing mole fraction of acetic acid present in the reacting system at any time as calculated from chemical shift data from the n.m.r. experiment and from the chemical experiment compared with the theoretical curves for a second order reaction with different assumed values of k_{II} . Symbols used in Fig. 2 and Fig. 3 are used here in the same sense.

With equimolecular solutions of pure acetic anhydride and water, only a few measurements on reaction rate have been described in the literature. As the results from these were not quite in agreement with each other and also as none was carried out under the same conditions as our n.m.r. experiment an actual chemical experiment was necessitated.

The chemical procedure

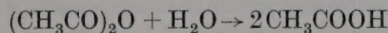
Equal numbers of millimoles of pure acetic anhydride and water were mixed and shaken for about 10 minutes until a single liquid phase was obtained.

At certain intervals samples were withdrawn by 1 cc pipet and analysed to determine the amount of acetic anhydride then left unreacted.

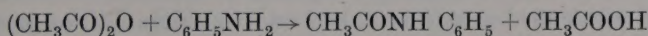
The titration procedure used was that originally recommended by Menshutkin and Wassilief (1889) [14]. Their method is, however, not sufficiently accurate, as pointed out by Treadwell [15]. The aniline titration method used by us is that modified by Caudri [16] and tested also by Vles [17].

Each sample for titration was added to 100 cc of an almost saturated solution of aniline in water, prepared by dissolving 25 cc of freshly distilled aniline per litre of water.

The acetic acid formed both in the slow reaction in question



and in the fast reaction taking place in the aniline solution



was titrated by standard alkali with phenolphthalein as indicator. All aqueous solutions were made of carbon dioxide-free water.

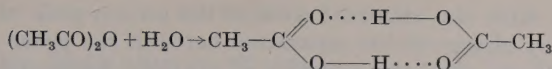
From one mole of acetic anhydride the first reaction will give two moles of acetic acid where the second reaction will give only one mole. Thus at the time t , in a solution of 1000 g, $2x$ moles of acetic acid are formed from the hydrolysis and $a - x$ moles from the reaction of acetic anhydride and aniline. The total amount of acetic acid is then $a + x$ moles. As a is known and $a + x$ can be determined by titration, x is obtained. Knowing the weights of the samples withdrawn for titration one can thus find out the molalities of the components at any time t . From the known values of a and x we can plot the mole fraction of acetic acid against time to compare it with n.m.r. and theoretical curves as presented in Figs. 3 and 4.

Discussion

In what follows we shall discuss the findings of the n.m.r. experiment on the kinetics of the hydrolysis of acetic anhydride, those found in the actual chemical analysis just described and the investigations of some other workers who used chemical or physical methods, e.g. conductivity measurements. As mentioned earlier, most of the investigators have studied the hydrolysis in dilute aqueous solutions. For conductivity measurements [18] as for many other physical methods the use of very dilute solutions is essential for their accuracy. In experiments with dilute aqueous solutions the hydrolysis behave like a pseudo-first-order reaction since the concentration of water remains virtually constant during the reaction. Few experiments have been done by chemical or other physical methods on the hydrolysis of acetic anhydride with equimolecular quantities of water and acetic anhydride without using any solvent at the outset. The experimental findings of the different investigators, using different procedures, are not quite in agreement with each other.

In their early work Menshutkin and Wassilief [14] studied the reaction using equimolecular quantities of acetic anhydride and water by dissolving the reactants in acetic acid to get one homogeneous phase. The question of the homogeneity of the liquid phase of the reactants at the outset of the reaction has also been discussed by us earlier. Menshutkin and Wassilief's experimental results were slightly in better accord with a first order reaction than with a second order one. Lindemann [19], however, in a recent study of the hydrolysis with equimolecular quantities of the reactants, using a better titration method, found that the rate of hydrolysis is neither in agreement with a first order reaction nor quite with a second order one. He pointed out that the approximate second order rate constant (at 25°C) increased during the reaction from 5×10^{-6} to $2.8 \times 10^{-5} \text{ sec}^{-1}$. From Fig. 3 it appears that the approximate k_{II} value of our titration experiment is 10^{-5} but with a tendency to increase during the reaction. It is reasonable that the k value may change as the reaction medium changes from dilute to concentrated acetic acid during the hydrolysis. From Figs. 2 and 3 it appears that the n.m.r. and chemical experimental observation are in fair agreement during the first part of the reaction until the mole fraction of acetic acid formed is 0.5, after which the observations of the two experiments are in disagreement. In the region where the disagreement is marked due to the increasingly high acetic acid concentration the effect of dimerisation of acetic acid should be taken into consideration, as mentioned in the introduction.

The argument presented above requires that for the region towards the end of the hydrolysis the reaction



and the molality

$$\alpha - x \qquad \alpha - x \qquad x$$

be taken into consideration.

The mole fraction of acetic acid dimer near the end of the reaction is $x/(2\alpha - x)$ and that of water is $(\alpha - x)/(2\alpha - x)$.

Now referring to the procedure adopted in the section "Analysis of n.m.r. data", the fraction of exchangeable protons in acetic acid dimer can be determined from the chemical shift data. This fraction, denoted by p , is equal to x/α . Thus the mole fraction of acetic acid dimer, $x/(2\alpha - x)$, is given by $p/(2 - p)$.

Remembering the restricted scope of applicability of this relation it can be used to calculate the mole fraction of acetic acid for the n.m.r. curve for times towards the end of the reaction. This procedure of determining the mole fraction of acetic acid from the dimerisation point of view must however also be taken into consideration in the titration experiment. We have seen that this procedure of calculating mole fractions of acetic acid for the n.m.r. and the titration experiments does not solve the disagreement between the two curves in the region where the mole fraction of acetic acid is greater than 0.5. However, the procedure outlined above shows that the mole fraction of acetic acid and the fraction of exchangeable protons (p) are not linearly related, at least not in the region where the concentration of acetic acid is high. But in the procedure adopted earlier, the mole fraction of acetic acid formed during the reaction, as calculated from Gutowsky and Saika's theory of chemical shift, is linearly related to the fraction of exchangeable protons in acetic acid. This change is primarily due to the consideration of dimerisation of acetic acid. Thus some departure of the experimental findings from the theoretical curves on reaction rates should arise if the mole fraction of acetic acid is calculated from Gutowsky and Saika's theory, which is not strictly applicable to systems of associated liquids like the acetic acid-water system. This may also be revealed from the nature of the plot of chemical shift against concentration of the acid in percentage by volume [6] (or concentration expressed in mole fraction).

Now from a system of acetic acid and water, in the absence of any acetic anhydride, an experimental observation of the chemical shift of the common peak due to protons of the COOH group and water from the CH₃ proton peak with respect to mole fraction of the acid can be obtained. Then a plot of chemical shift against fraction of exchangeable protons in acetic acid can be drawn. This chemical shift curve can be used (as a calibration curve) to determine approximately p which gives the mole fraction of acetic acid formed in a system of acetic anhydride, water and acetic acid. Even by adopting this procedure it has been found that the curves representing mole fractions of acetic acid against time according to n.m.r. and chemical analysis are not in agreement in regions where the concentration of the acid is high and the questions of dimerisation of acetic acid and complex formation between water and acetic acid arise.

The question whether acetic anhydride, like acetic acid, also forms dimers and other complexes with acetic acid and water is rather doubtful [20]. A n.m.r. experiment with a sample of acetic acid and acetic anhydride shows that the separation between the proton peaks from COOH group and CH₃ group is the same as that from pure acetic acid. Since complex formation between acetic acid and acetic

anhydride would alter the chemical shift of the proton peak of the COOH group, the absence of any change in the separation between the peaks from COOH group and CH₃ group shows that the question of complex formation or association between acetic acid and acetic anhydride molecules may be ruled out.

The chemical shift in the n.m.r. experiment is susceptible to complex formation. Since the mole fraction of acetic acid present at any time in the reacting system is calculable from the actual chemical shift of the n.m.r. observations and since in the chemical analysis the mole fraction of acetic acid is known from titration, determining the number of single molecules and not any quantity related to the association of the acid molecules, it seems clear that the results of n.m.r. and chemical analysis will disagree in the region where the phenomenon of molecular association comes into play.

The chemical shift in the n.m.r. method may be suitably applied to study reactions in liquid systems of not too complicated a nature. It is applicable to study reactions in concentrated solutions where many other methods are not accessible. The nuclear magnetic resonance phenomenon may also be applied to studies of the kinetics of the keto-enol transformation in tautomeric mixtures.

Summary

Chemical shift in nuclear magnetic resonance phenomenon has been applied to study the kinetics of the hydrolysis of acetic anhydride using equimolecular quantities of the reactants. The quantity of acetic acid present at any time is calculated from chemical shift data from the n.m.r. experiment using Gutowsky and Saika's theory of chemical shift. From the analysis of n.m.r. observations the specific reaction rate for a first order reaction was found to be approximately $6 \times 10^{-5} \text{ sec}^{-1}$ at 27°C. The n.m.r. observations have been compared with an actual chemical analysis performed with the same concentrations of the reactants and at the same temperature. The n.m.r. and chemical experimental observations are in fair agreement during the first part of the reaction until the mole fraction of acetic acid formed is 0.5, after which the observations of the two experiments are in disagreement. The observations of the titration experiment are in better agreement with a second order reaction than a first order one. Causes of this disagreement are partly attributed to molecular association and complex formation in the reacting liquid system and to the approximate validity of Gutowsky and Saika's theory of chemical shift. The applicability of chemical shift effects in the n.m.r. phenomenon to studies of kinetics of chemical reactions have been discussed.

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